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Echocardiographic predictors of atrial fibrillation recurrence after catheter ablation: A literature review

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Abstract

Background: *Catheter ablation (CA) is a well-known treatment option for patients with symptomatic drug-resistant atrial fibrillation (AF). Multiple factors have been identified to determine AF recurrence after CA, however their predictive value is rather small. Identification of novel predictors of CA outcome is therefore of primary importance to reduce health costs and improve long-term results of intervention. The recurrence of AF following CA is related to severity of left ventricular (LV) dysfunction, extent of atrial dilatation and fibrosis. The aim of this paper was to present and discuss the latest studies on the utility of echocardiographic parameters in terms of CA effectiveness in patients with paroxysmal and persistent AF.*

Methods: *PubMed, Google Scholar, EBSCO databases were searched for studies reporting echocardiographic preprocedural predictors of AF recurrence after CA. LV systolic and diastolic function, as well as atrial size, strain and dyssynchrony were taken into consideration.*

Results: *Twenty one full-text articles were analyzed, including three meta-analyses. Several echocardiographic parameters have been reported to determine a risk of AF recurrence after CA. There are conventional methods that measure left atrial size and volume, LV ejection fraction, parameters assessing LV diastolic dysfunction, and methods using more innovative technologies based on speckle tracking echocardiography to determine left atrial synchrony and strain. Each of these parameters has its own predictive value.*

Conclusions: *Regarding CA effectiveness, every patient has to be evaluated individually to estimate the risk of AF recurrence, optimally using a combination of several echocardiographic parameters.* (Cardiol J 2020; 27, 6: 848–856)

Key words: atrial fibrillation, catheter ablation, pulmonary vein isolation, echocardiography, predictors, recurrence

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia with a projected prevalence of 14–17 million by the year 2030 in the European Union [1]. AF remains one of the major causes of stroke, heart failure, sudden death, and cardiovascular morbidity. With large increases in the burden of AF expected in the coming decades, better diagnosis and stratification of treatment selection is of paramount importance.

In recent years catheter ablation (CA) became a common treatment for patients with symptomatic, drug-resistant AF. The success rate of CA, defined as no AF relapse, of up to 70% for patients with paroxysmal AF and around 50% in those with persistent AF [1]. Multiple factors have been identified for AF recurrence after CA, such

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as age, AF duration, ventricular and atrial function and comorbidities, however their predictive value is rather small [1, 2]. Therefore, new predictors of procedural outcome are needed for better identification of the most suitable candidates for CA.

Optimal patient selection is crucial to avoid unnecessary risk associated with CA, which can be accompanied by serious complications such as cardiac tamponade, stroke, pulmonary vein stenosis and atrio-esophageal fistula. Finally more accurate prediction can influence a decision for continuation of long-term oral anticoagulant and antiarrhythmic drug therapy.

Much of the information on ventricular and atrial function can be derived from cardiac magnetic resonance and tomography, but for practical reasons echocardiography is mostly used in clinical settings. Active deformation of the heart muscle during the cardiac cycle can be assessed with strain imaging from two-dimentional speckle tracking echocardiography (STE). This technique enables the recognition of subtle cardiac dysfunction and markers myocardial damage. The ultimate goal of these markers is to define different types of AF that are characterized by specific pathophysiology which may warrant early aggressive intervention and will respond favourably to CA. Recurrent AF after CA seems to be higher in patients with signs of atrial cardiomyopathy, also ventricular function plays a major role in the efficacy of this procedure.

The aim of this paper was to present and discuss the latest studies on echocardiographic parameters in terms of CA effectiveness in the treatment of patients with paroxysmal and persistent AF.

PubMed, Google Scholar, EBSCO databases were searched using the key words "echocardiographic predictors of atrial fibrillation after catheter ablation" or "echocardiography atrial fibrillation," "echocardiography pulmonary vein isolation" or "echocardiography catheter ablation." The search returned 104 abstracts, published from 1997 to 2017, all in English. After screening the abstracts, 42 were included for full-text analysis, according to their relevance to the subject. The criteria to include studies were as follows: (A) patients with paroxysmal or persistent AF referred for CA, (B) endpoint analysis taking into account the first recurrence of AF (defined as any documented episode of AF lasting > 30 s). Finally, 21 full-text articles were included in relation to CA in patients with AF. The following echocardiographic criteria were taken into consideration: left (LA) and right atrial (RA) size (diameter, area and volume), left ventricular (LV) ejection fraction (LVEF), parameters assessing LV diastolic dysfunction, atrial strain and dyssynchrony (Table 1).

Methods

Atrial size

It is established that LA size contributes to structural remodeling and therefore to atrial fibrosis [3]. Dilatation of the LA is an independent predictor of new onset AF [4]. It is also a well-known predictor of low success for CA in terms of AF recurrence [5–7].

Zhuang et al. [8] performed a meta-analysis of 22 studies which included over 3700 patients, which showed that an increased antero-posterior diameter of the LA was associated with a higher risk of AF recurrence after CA. The antero-posterior diameter of LA before CA, obtained from the parasternal long-axis view, was 35–50 mm. In patients with arrhythmia recurrences it was 1.87 mm larger than in those with successful pulmonary vein isolation [8]. According to European expert consensus from 2012 the LA diameter over 50–55 mm indicates limited success of CA [6]. In a study performed by Liao et al. [9] on 589 patients with paroxysmal AF, LA diameter over 43 mm and LV systolic diameter over 31 mm were the best cut-off values for predicting AF progression after CA. Their predictive value was highest when both of the above-mentioned diameters were exceeded [9]. LA dilation can be asymmetric and the antero-posterior dimension underestimates and does not truly reflect LA size. Studies focusing on LA area, however, did not confirm its predictive utility. Tomas at al. [10] found that LA area > 24 cm^2 did not predict AF recurrence at 12 month follow up. Njoku et al. [11] in a meta-analysis of 21 observational studies encompassing 3850 patients reported that patients with AF recurrence had larger mean left atrial volume (LAV) and LAV index (LAVi) compared to patients with no arrhythmia relapse. Moreover, they found that increased LAV/LAVi was independently associated with frequent AF recurrences after CA. There was a 3% increase in the odds of AF relapse per unit increase in LAV/LAVi. Shin et al. [12] found that LAVi of 34 mL/m^2 showed a sensitivity of 70% and a specificity of 91% to predict AF recurrence.

Atrial fibrillation is a biatrial disease. RA, with its enlargement and remodeling also involved in AF relapse [13]. Moon et al. [13] reported that increased RA volume index (RAVi) might affect early AF recurrence (within 3 months) after CA and RAVi over 78 mL/m^2 predicted the early recurrence with

Table 1. Studies about the predictive echocardiographic factors of atrial fibrillation recurrence post-catheter ablation.

Total patients (n)	Study type	Paroxysmal AF (n)	Persistent AF (n)	LVEF [%]	Median follow-up [months]	AF recurrences after CA (n)	Prognostic ECHO parameter	Reference
ARIAL SIZE								
3750 (22 studies)	Meta--analysis	2274	1476	NS	6–30 ± 13	NS	LAD was 1.87 mm higher in patients with arrhythmia recurrences	Zhuang et al. 2011
1425 (9 studies)	Meta--analysis	611	544	> 50	17 (mean)	NS	Higher mean LAVi (using ECHO, CT, or MRI)	Njoku et al. 2017
1559 (11 studies)	Meta-analysis	913*	537*	> 50	17 (mean)	NS	Higher mean LAV (using ECHO, CT, or MRI)	
2886 (13 studies)	Meta-analysis	1932	960	> 50	18	NS	Higher mean LAV/LAVi (using ECHO, CT, or MRI)	
470	Retrospective	196	274	> 50	24.3 ± 18	284 (60.6%)	RAD > 35.5 mm (in PAF with LAD > 35 mm)	Nan Wen et al. 2017
LEFT VENTRICULAR SYSTOLIC DYSFUNCTION								
368	Retrospective	170	198	≤ 40 (111 patients), > 50 (157 patients with isolated LVDD), 100 patients with normal LV function	13	NS	LVEF ≤ 40%	Cha et al. 2011
230	Retrospective	80	150	< 50 (97 patients), ≥ 50 (133 patients)	11	NS	LVEF was not a risk factor	Black-Maier et al. 2017
363	Prospective	118	245	≤ 35	37.8	60 (37%)	LVEF ≤ 25%	Marrouche et.al. 2018
LEFT VENTRICULAR DIASTOLIC DYSFUNCTION								
198	Retrospective	173	25	> 50	12	76 (38%)	Average E/e' > 13 (during sinus rhythm)	Hirai et al. 2014
215	Prospective	113	102	> 50	12 ± 6	38 (18%)	Average E/e' > 14	Masuda et al. 2017
22	Retrospective	5	17	> 50	21 ± 12	9 (41%)	E/e' ≥ 15	Okamatsu et al. 2015

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Table 1 (cont.). Studies about the predictive echocardiographic factors of atrial fibrillation recurrence post-catheter ablation.

Total patients (n)	Study type	Paroxysmal AF (n)	Persistent AF (n)	LVEF (%)	Median follow-up [months]	AF recurrences after CA (n)	Prognostic ECHO parameter	Reference
232	Retrospective	152	80	> 50	36	59 (25%)	LVDD defined as: septal e″< 8 lateral e″ < 10 LAV ≥ 34 mL/m^2 (risk factor of VLR)	Onishi et al. 2017
124	Prospective	70	54	> 50	12	42 (34%, early- during first week after PVI), 26 (27%, late)	E/A ratio (in early recurrence)	Kosiuk et al. 2014
LEFT ATRIAL STRAIN								
686 (8 studies)	Meta-analysis	529	157	> 50	11	232 (94.9%)	LA strain < 22.8% (using QRS or P analysis, using different software packages)	Ma et al. 2016
100	Retrospective	68	32	> 50	12	26 (26%)	Basal LA lateral strain < 25.3%	Yasuda et al. 2015
102	Retrospective Prospective	0	102	> 50	15	57 (56%)	LA strain < 10% (during an episode of persistent AF)	Parwani et al. 2017
42	Prospective	42	0	> 50	14 ± 7	12 (29%)	LA global peak area strain (3D-GASs) < 28.9% (measured in systole, determined by 3D speckle tracking)	Mochizuki et al. 2017
OTHER PARAMETERS								
25	Retrospective	25	0	> 42	20 ± 9	7 (28%)	LA mechanical dyssynchrony (speckle tracking strain analysis)	Loghin et al. 2013
132	Retrospective	132	0	> 50	23 ± 7	38 (28.8%)	FMR ≥ 1 (regurgitation jet area to LA area during sinus rhythm)	Qiao et al. 2016

*1 study not stated; 3D-GASs —left atrial global peak area strain in systole determined by three-dimensional speckle tracking echocardiography; A — late mitral inflow velocity assessed by pulsed wave Doppler; AF — atrial fibrillation; CA — catheter ablation; CT — computed tomography; E — early mitral inflow velocity assessed by pulsed wave Doppler; E/A — mitral early to late diastolic peak ratio assessed by pulsed wave Doppler; e' — early diastolic mitral annular velocity assessed by tissue Doppler; e' — early diastolic mitral annular velocity assessed by tissue Doppler; FMR — functional mitral regurgitation; LA — left atrium; LAD — left atrial diameter; LAV — left atrial volume; LAVi — left atrial volume index; LV — left ventricular; LVDD — left ventricular diastolic dysfunction; LVEF — left ventricular ejection fraction; MRI — magnetic resonance imaging; n — number of patients; PAF — paroxysmal AF; PVI — pulmonary vein isolation; RAD — right atrial diameter assessed in the 4-chamber apical view; VLRs — very late recurrences (> 12 months)

74% sensitivity and 68% specificity [13]. Wen et al. [14] found that RA size predicted successful CA in patients with paroxysmal AF and LA horizontal diameter (determined as the measurement from the middle of mitral isthmus to the LA roof in the 4-chamber apical view) enlargement over 35 mm. RA was measured from the middle of tricuspid isthmus to the RA roof in the 4-chamber apical view, and when this diameter was below 35.5 mm it predicted AF recurrence-free survival at over 2-year follow up. Although a large cohort (over 400 patients) was examined, the results might be applicable only to an Asian population.

Left ventricular systolic function

In previous years several trials comparing amiodarone with CA in AF patients with heart failure (HF) and reduced ejection fraction (HFrEF) showed ablation to be superior at maintaining sinus rhythm [15, 16]. However the efficacy of CA in HFrEF patients with AF is still a matter of debate. Development of AF in HFrEF patients occurs due to eccentric remodeling of the LA. In this group an increase in LA diameter and volume was observed. The underlying electrical substrate driving to AF is likely different than in patients with HF and preserved ejection fraction, where LA stiffness is dominant [17].

In a study performed by Cha et al. [18] three groups of patients with AF undergoing CA were analyzed: 111 with LV systolic dysfunction (LVEF ≤ 40%), 157 with isolated LV diastolic dysfunction (LVEF > 50%) and 100 individuals with normal LV function. The authors reported that AF elimination rate was significantly lower in patients with systolic dysfunction (62%, $p = 0.002$) and non-significantly lower in those with diastolic dysfunction (75%, $p = 0.15$) when compared with the group with normal LV function.

Black-Maier et al. [16] compared two groups of about 100 patients with LVEF of less and over 50% and showed no significant differences in the rates of atrial arrhythmia recurrence between HF patients with preserved and reduced ejection fraction (33.9% vs. 32.6%; $p = 0.8$) at 1-year follow up. The contradictory result may be due to differences in the study population enrolled. Patients in the Black-Maier et al. [16] study were older and were more likely to have hypertension and diabetes mellitus.

The efficacy of CA in patients with HFrEF and AF was uncertain, until the lately published breakthrough CASTLE-AF trial [19]. It was a multicenter, randomized, controlled trial to assess whether CA lowers morbidity and mortality as compared with medical therapy (rate or rhythm control) in patients with coexisting AF and medically managed HF. The study included almost 400 patients with symptomatic paroxysmal or persistent AF and HF in the New York Heart Association class II–IV, LVEF of 35% or less and an implanted defibrillator. Mortality and hospitalization for worsening HF was significantly reduced in patients treated with CA. After 5 year follow-up sinus rhythm was maintained in 63% of patients in the ablation group vs. 22% in the medically treated group ($p < 0.001$). The study also revealed that patients with LVEF of less than 25% were less likely to benefit from ablation than those with LVEF between 25% and 35%. It would be interesting to determine the success rate of CA in patients with advanced HF but preserved ejection fraction.

Left ventricular diastolic dysfunction

Left ventricular diastolic dysfunction may indicate an increase in LV filling pressure, which can influence LA remodeling over the long term [20]. Wall stress due to increased atrial pressure plays an important role in the development of atrial electrical and structural remodeling. Impaired diastolic function has also been reported to be associated with AF recurrences [21]. According to guidelines of the American Society of Echocardiography, LV diastolic dysfunction can be evaluated and graded by mitral inflow assessed by pulsed wave Doppler, tissue Doppler of LV walls, and LA size [22].

In 2014 Hirai et al. [23] reported that elevated LA pressure, as determined by increased average E/e' index (E — early transmitral flow velocity obtained by pulsed wave Doppler; e'— early diastolic mitral velocity measured by tissue Doppler; averaged annular septal and lateral values), was the only echocardiographic parameter that predicted AF recurrence after CA. The E/e' value over 13 indicated increased risk of AF relapse during 12 month follow up.

Three years later Masuda et al. [24] reported that patients with E/e' > 14 before CA more frequently developed recurrent atrial tachyarrhythmias after single and multiple procedures. It was the first study demonstrating that patients with high E/e' ratio, along with age, female sex, low body mass index, and persistent AF more frequently presented low-voltage areas within the LA predisposing to AF, when endocardial voltage mapping was performed during the CA procedure. The relationship between higher E/e' ratio and the presence of low voltage areas in the LA may indicate

that higher E/e' is associated with advanced atrial arrhythmogenic substrate outside the pulmonary veins. This might explain AF recurrences even after a properly performed (without reconnections) pulmonary vein isolation.

Finally Okamatsu et al. [25] who examined 24 patients with hypertrophic cardiomyopathy demonstrated that E/e' ratio was the only predictor of AF recurrence following pulmonary veins isolation (PVI). Patients with E/e' ≥ 15 had a significantly higher risk of AF recurrence than those with E/e' < 15. Thus, patients with AF and mild or moderate LV diastolic dysfunction (E/e' < 15) are better candidates for PVI than those with a restrictive inflow pattern.

In a study performed by Onishi et al. [26] LV diastolic dysfunction at baseline was the only independent risk factor of late AF recurrence, defined as first AF relapse after more than 12 months subsequent to CA. The authors defined LV diastolic dysfunction very strictly and patients had to fulfill all three of the following criteria: early diastolic septal annular velocity e' < 8 cm/s, lateral annular velocity e' < 10 cm/s and LAVi ≥ 34 mL/m^2. After a single CA procedure, reconnections of pulmonary veins could affect recurrence of AF. To minimize the influence of pulmonary vein reconnections, risk factors of late recurrences after multiple CA procedures, not only after a single session were examined. LV diastolic dysfunction appeared to be the only risk factor of late AF relapses.

Kosiuk et al. [27] showed that E/A mitral inflow pattern (early to late mitral inflow velocity ratio, assessed by pulsed-wave Doppler at the level of the mitral valve), which is associated with LV diastolic dysfunction, was the best pre-procedural predictor of short-term AF recurrence during the first week after PVI. An E/A ratio of 1.35 was the cut-off value with the highest sensitivity and specificity for predicting early AF recurrence. In contrast to Onishi et al. [26], the authors reported that none of the parameters evaluating LV diastolic function predicted long-term PVI result (defined as any documented AF episode within a 3–12 month period after ablation). This discrepancy may be due to different definitions of LV diastolic dysfunction applied in both studies. Moreover, Kosiuk et al. [27] analyzed the results of CA after only a single procedure, and it can also explain the contradictory results because, as mentioned above, late AF recurrences are mainly due to pulmonary vein reconnections [28, 29]. Finally, a limited number of patients with severe LV diastolic dysfunction might preclude evaluation of other parameters, like E/e' ratio as predictors of both, short- and long-term AF recurrences after CA.

Left atrial strain

Schneider et al. [30] evaluated results of tissue Doppler imaging (TDI)-based LA strain analysis in patients with AF for the prediction of successful CA. The authors showed that patients with higher atrial strain and strain rate after CA appear to have a greater likelihood of maintaining sinus rhythm. Peak strain and strain rate were measured at each mid-LA segment one day prior to, within 24 hours, and 3 months after CA. A value of 20% for atrial septal systolic strain obtained before the procedure predicted sinus rhythm maintenance after CA, but with rather low sensitivity (57%) and specificity (56%). This method, however, is prone to angulation error and suffers from variable reproducibility. Moreover, it does not allow distinguishing active myocardial contraction from its passive motion.

Two-dimensional STE (2D-STE) is angle independent and thus more useful for LA strain analysis [31]. There are several studies indicating that LA strain has higher predictive value than LA size obtained from conventional echocardiography [31, 32]. The LA strain reflects LA reservoir, conduit and booster pump function. Furthermore, it correlates with the extent of LA fibrosis, especially in patients with persistent AF [7, 33].

A meta-analysis of 8 studies, which included 686 patients with paroxysmal AF showed that global LA strain is useful to identify individuals at high risk of AF recurrence after CA [34]. This analysis included both patients with sinus rhythm or AF at baseline, before PVI. In the group with AF, the beginning of QRS was set as the zero strain point. In patients with sinus rhythm the trigger for strain analysis was put either at the onset of QRS complex or P-wave. LA peak positive strain of less than 22.8% predicted AF recurrence with 78% sensitivity and 75% specificity. These results were independent of the applied method of LA strain analysis: from the beginning of QRS or P-wave, as well as software package used.

Left atrial strain measured on LA lateral wall by 2D-STE might be the most useful parameter for predicting successful AF ablation as it represents pure LA contractile function [35]. Yasuda et al. [35] indicated a significant prognostic value of basal LA lateral total strain, both in patients with sinus rhythm and AF during examination. The authors set the zero strain point at the beginning of QRS complex in the group with AF and at P wave in the group with sinus rhythm. The total strain

was calculated as follows: positive peak strain – negative peak strain. They reported that a value below 25.3% in basal LA lateral strain showed 81% sensitivity and 72% specificity for predicting AF recurrence after CA [35].

Most of the studies included in the mentioned meta-analysis [34] assessed patients with mainly paroxysmal or different types of AF. Parwani et al. [36] reported that low LA peak positive strain (< 10%) during an episode of persistent AF was strongly linked to recurrence of AF after one or even after two CA procedures.

Finally, some results suggest that three--dimensional STE (3D-STE) is potentially more accurate than 2D-STE for assessment of LA dysfunction in patients with AF [37, 38]. Mochizuki et al. [39] assessed patients with paroxysmal AF and found that global LA strain determined by 3D-STE less than 28.9% was a predictor of AF recurrence after the first-time CA Moreover, 3D-STE global LA strain was a better predictor of AF relapse after CA than LA strain obtained by 2D-STE. Three-dimensional strain analysis reflects LA function in many directions: not only longitudinal, but also circumferential and area strains. This can explain its superiority over 2D-STE.

Left atrial mechanical dyssynchrony

The LA mechanical dyssynchrony, which clearly indicates the presence of atrial structural and electrical remodeling, can predict recurrence of AF after CA in patients with paroxysmal AF [40, 41]. It can be determined by different echocardiographic methods.

Den Uijl et al. [41] reported that total atrial conduction time (PA-TDI), reflecting atrial electrical remodeling, was an independent predictor of AF recurrence after PVI. Total atrial conduction time was obtained by measuring the time delay between the onset of the P-wave on the surface electrocardiogram and the peak A'-wave of spectral tissue Doppler tracing on LA lateral wall. The prolonged value of 146 ± 20 ms was associated with AF recurrence after CA (for comparison PA-TDI in healthy subjects was 78 ± 7 ms) [42]. Similarly, Fukushima et al. [43] found that PA-TDI was an independent predictor of AF recurrence in patients with paroxysmal AF. They reported 2.5--fold higher rate of AF relapses in patients with PA-TDI duration > 151.3 ms. Evranos et al. [44] demonstrated a relationship between PA-TDI on LA lateral wall and recurrence of AF in patients treated with cryobaloon ablation. PA-TDI over 125 ms predicted AF recurrence with 80% sensitivity and 90% specificity. Unlike den Uijl et al. [41] they defined PA-TDI as a time interval from the onset of P wave on the surface electrocardiogram to the beginning of the A' wave.

Loghin at al. [40], used an algorithm based on 2D-STE — the vector velocity imaging (VVI) and looked at the timing of peak longitudinal strain obtained on opposing LA walls during atrial contractile phase. They found that maximum opposing walls delay of over 51 ms predicted AF recurrence after CA with 89% sensitivity and 72% specificity. Unfortunately, the study was retrospective and based on a small cohort of 25 patients.

Sarvari et al. [45] measured the dispersion of LA contraction duration, defined as the time difference from the peak of P wave on the surface electrocardiogram during sinus rhythm to maximum LA shortening assessed by 2D-STE strain (peak negative longitudinal strain). The standard deviation of contraction durations measured in 18 LA segments was defined as LA mechanical dispersion. The authors reported that patients with AF relapse and normal (LAV 25 ± 10 mL/m^2) presented with significantly greater LA mechanical dispersion compared with patients after successful CA (38 ± 14 ms vs. 30 ± 12 ms; $p < 0.001$). Therefore LA mechanical dispersion can be a useful tool to predict AF recurrence after CA in patients with structurally normal heart.

Functional mitral regurgitation

Qiao et al. [46] reported that functional mitral regurgitation, defined as regurgitation jet area to LA area ratio ≥ 0.1 in subjects without any primary valvular disease, independently predicted long-term outcomes post ablation in patients with paroxysmal AF. Functional mitral regurgitation was strongly correlated with the presence and extent of low voltage zones within the LA, assessed invasively prior to ablation.

Conclusions

Several echocardiographic parameters have been reported to determine the risk of AF recurrence after CA. These parameters reflect morphology, function and myocardial remodeling in patients with AF. There are conventional methods that measure LA size and volume, LVEF, parameters assessing LV diastolic dysfunction, and methods using more innovative technologies based on STE to determine LA synchrony and strain. Each of these parameters has their own predictive value. Unfortunately, there is no single parameter that

actually enables the prediction of AF relapse after CA. To summarize, the predictors of AF recurrence after CA which were confirmed by several groups were LA diameter > 50–55 mm or LAVi > 34 mL/m^2, E/e' > 13–15, LA strain assessed by STE < 20–25% and total atrial conduction time measured by TDI > 150 ms. The presence of LV systolic dysfunction also lowered CA success rate with a bottom LVEF cut-off value of < 25%. It needs underlining that risk of AF recurrence after CA should be estimated individually, optimally on the basis of several echocardiographic parameters.

Conflict of interest: None declared

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